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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,572	12/30/2003	Richard B. Borgens	P01254-US-01 (19232.0011)	8077

7590 05/09/2006

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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,572	BORGENS, RICHARD B.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 9, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted December 29, 2005. This application claims benefit of provisional application 60/437104, filed December 30, 2002.

Claims 1-19 are put forth for consideration.

Applicant's amendment submitted December 29, 2005 is acknowledged wherein a minor typographical error in claim 12 is corrected.

Applicant's arguments received December 25, 2005 are deemed to be persuasive. Accordingly, rejections previously made under 35 USC 102 and 103 are withdrawn.

Claim rejections – 35 USC § 112

Claims 1-3 and 5-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 both include as one step of the claimed method, "administering a purine nucleoside **or analog thereof** to the patient." Claims 2-3, 5-12, and 14-19 depend from these claims and fail to further define the purine nucleoside or analog thereof This phrase does not clearly and distinctly indicate which molecules the Applicant regards as derivatives or analogs of a purine nucleoside. In common usage, this language may refer to any, all, or none of the following:

1) Modification of the recited compounds with protecting groups

2) Substitution of existing functional groups by equivalent functional groups

3) Replacement of a limited number of functional groups with nonequivalent functional groups.

As the specification fails to define the term "analog thereof," the language of these claims is indefinite.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Benowitz (US patent 6551612, Reference cited in PTO-1449) Benowitz teaches, "A method of treating a mammal having suffered a spinal cord injury which comprises intrathecal administration of a pharmaceutical composition to said mammal, **wherein the active ingredient comprises inosine**," further limited to administration of the pharmaceutical composition, "from the time of the spinal cord injury to 100 hours after the spinal cord injury." (Claim 2, also described in column 2, lines 13-30) Elsewhere, the

purines inosine and guanosine are both named as preferred pharmaceutical compounds for use in the invention of Benowitz. (Column 5, lines 26-30) This method comprises administering the same compound to the same patient population as the invention of instant claims 14-15.

Thus the claimed invention is anticipated by Benowitz.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Baranowitz (PCT international publication WO01/08691, Reference cited in PTO-892) Baranowitz discloses a method of regenerating mammalian tissues and organs by causing destabilization, transdifferentiatiation, and stabilization of mammalian cells from the site of injury. (P. 5, lines 28-31, p. 8, lines 29-30) Although not mentioned specifically, the spinal cord is included within the range of organs which could be regenerated by this method. One preferred embodiment of the invention of Baranowitz includes the administration of guanosine as the agent which causes transdifferentiation. (p. 11, lines 6-7) In one embodiment, the method of Baranowitz is practiced by the administration of a treatment capable of dedifferentiating mammalian cells, such as those described from p. 9, line 18 – p. 10, line 4 of Branaowitz, followed by the concurrent administration of guanosine (p. 11, lines 6-7) and a stabilizing agent, such as

those listed on p. 11, lines 8-10. The features of this therapeutic regimen beyond the administration of guanosine (i.e. pre-treatment of the site of injury to cause destabilization, and treatment with a stabilizing agent) are accurately described as, "conditions effective to restore nerve function through said spinal cord," and, "conditions effective to stimulate nerve regeneration at the site of the spinal cord injury." In the language of instant claims 14-15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-8, 10-13, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benowitz (US patent 6551612, Reference cited in PTO-1449) in view of Borgens et al. (US patent 4919140, Reference included with PTO-892) Benowitz teaches, "A method of treating a mammal having suffered a spinal cord injury which comprises intrathecal administration of a pharmaceutical composition to said mammal, **wherein the active ingredient comprises inosine**," further limited to administration of the pharmaceutical composition, "from the time of the spinal cord injury to 100 hours after the spinal cord injury." (Claim 2, also described in column 2, lines 13-30) Elsewhere, inosine and guanosine are both named as preferred pharmaceutical compounds for use in the claimed invention (Column 5, lines 26-30) Furthermore,

Benowitz et al. also teaches that the purine nucleosides may be administered over a sustained period by the use of an infusion pump, which is an implanted device in the language of instant claim 8. Although Benowitz does not explicitly specify that the endpoint of the claimed therapeutic method is one, "wherein nerve function through said injured spinal cord is at least partially restored," in the language of instant claim 1, or wherein restoration of nerve function is evidenced by one or more of the therapeutic endpoints described in instant claim 12, the achievement of these therapeutic endpoints, particularly restoration of nerve function, nerve impulse conduction, and an increase in reflex behavior, is an essential part of a successful treatment for a spinal cord injury. A therapeutic regimen which did not accomplish any of these improvements in the patient's condition could not be said to constitute treatment of the injury. Benowitz does not teach the concurrent administration of an electrical stimulus to the site of injury.

Borgens et al. discloses an oscillating field stimulation device described as, "An apparatus for stimulating nerves in the central nervous system of a mammal to regenerate within the central nervous system, comprising means for generating an oscillating electrical field with a polarity reversal period long enough to stimulate growth of cathodally facing axons of the nerves to be stimulated but less than a die back period of anodally facing axons of the nerves to be stimulated." (Claim 7) This device is intended to be used to promote the regeneration of an injured spinal cord, and falls within the limits of the terms, "electrically stimulating the site of the spinal cord injury," a

device which electrically stimulates the site of the spinal cord injury," and "an oscillating field stimulation device," as they occur in the instant claims.

It would have been obvious to one of ordinary skill in the art at the time of the invention to simultaneously treat a patient having suffered a spinal cord injury by administering purine nucleosides according to Benowitz. while also administering electrical stimulus by implanting the device of Borgens et al. into the patient. It would also have been obvious to one of ordinary skill in the art to manufacture a kit according to claims 16-19 comprising an infusion pump for the intrathecal delivery of inosine and/or guanosine, an oscillating field stimulation device according to Borgens et al., and written instructions describing a method of using these two devices concurrently to treat a central nervous system injury, specifically a spinal cord injury.

One of ordinary skill in the art at the time of the invention would be motivated to combine the inventions in this way in order to better treat patients suffering from injury to the spinal cord. One of ordinary skill in the art would have reasonably expected that, because administration of purine nucleosides and oscillating field stimulation were both known to be useful independently for the treatment of spinal cord injuries, concurrently administering both therapies would produce additive effects.

It has been held that it is *prima facie* obvious to combine two inventions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third invention for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Moreover, with respect to the instructions that direct one how to use a kit, the US court of appeals for the Federal Circuit, *In re Ngai* 03-1524, has ruled that a kit of the prior art with a set of instructions is unpatentable (See the precedential opinion issued May 13, 2004).

Thus the invention taken as a whole is *prima facie* obvious.

Claims 1-3, 5-7, 9-13, and 16-19 are rejected under 35 U.S.C. 103 as being unpatentable over Baranowitz (PCT international publication WO01/08691, Reference cited in PTO-892) In view of Borgens et al. (US patent 4919140, Reference included with PTO-892) Baranowitz discloses a method of regenerating tissues and organs in a mammal by causing destabilization, transdifferentiatiation, and stabilization of mammalian cells from the site of injury. (P. 5, lines 28-31, p. 8, lines 29-30) Although not mentioned specifically, the spinal cord is included within the range of organs which could be regenerated by this method. One preferred embodiment of the invention of Baranowitz includes the administration of guanosine as the agent which causes transdifferentiation. (p. 11, lines 6-7) In one embodiment, the method of Baranowitz is practiced by the administration of a treatment capable of dedifferentiating mammalian cells, such as those described from p. 9, line 18 – p. 10, line 4 of Branaowitz, followed by the concurrent administration of guanosine (p. 11, lines 6-7) and a stabilizing agent, such as those listed on p. 11, lines 8-10. As parent claim 1 is directed to, "A method for treating a patient having a spinal cord injury, the method **comprising**: electrically stimulating the site of the spinal cord injury; and administering a purine nucleoside or

analog thereof to the patient," the features of this therapeutic regimen beyond the administration of guanosine (i.e. pre-treatment of the site of injury to cause destabilization, and treatment with a stabilizing agent) are included as possible additional elements in the claimed invention. In particular, the use of trauma to destabilize the target tissue, as described on p. 10 of Baranowitz, lines 5-31, would include the surgically induced trauma involved in the implantation of an infusion pump and an oscillating field device at the site of injury, as described by instant claims 2, 3, and 8. Baranowitz does not disclose any limitations as to the age of the injury to be treated, so the treatment of injuries more than three months old according to claim 9 falls within the limitations of Baranowitz.

Although the examples given (e.g. pp. 18-22) involve the oral administration of the therapeutic agents (as described in instant claims 5-6), intrathecal or other local administration (as described in claim 7) is expected to be equally effective as the purine nucleoside is active at the site of injury. Although Benowitz does not explicitly specify that the endpoint of the claimed therapeutic method is one, "wherein nerve function through said injured spinal cord is at least partially restored," in the language of instant claim 1, or wherein restoration of nerve function is evidenced by one or more of the therapeutic endpoints described in instant claim 12, the achievement of these therapeutic endpoints, particularly restoration of nerve function, nerve impulse conduction, and an increase in reflex behavior, is an essential part of a successful treatment for a spinal cord injury. A therapeutic regimen which did not accomplish any of these improvements in the patient's condition could not be said to constitute

treatment of the injury. Benowitz does not teach the concurrent administration of an electrical stimulus to the site of injury.

Borgens et al. discloses an oscillating field stimulation device described as, "An apparatus for stimulating nerves in the central nervous system of a mammal to regenerate within the central nervous system, comprising means for generating an oscillating electrical field with a polarity reversal period long enough to stimulate growth of cathodally facing axons of the nerves to be stimulated but less than a die back period of anodally facing axons of the nerves to be stimulated." (Claim 7) This device is intended to be used to promote the regeneration of an injured spinal cord, and falls within the limits of the terms, "electrically stimulating the site of the spinal cord injury," a device which electrically stimulates the site of the spinal cord injury," and "an oscillating field stimulation device," as they occur in the instant claims.

It would have been obvious to one of ordinary skill in the art at the time of the invention to simultaneously treat a patient having suffered a spinal cord injury by administering purine nucleosides according to Baranowitz. while also administering electrical stimulus by implanting the device of Borgens et al. into the patient.

One of ordinary skill in the art at the time of the invention would be motivated to combine the inventions in this way in order to better treat patients suffering from injury to the spinal cord. One of ordinary skill in the art would have reasonably expected that, because administration of purine nucleosides and oscillating field stimulation were both known to be useful independently for the treatment of spinal cord injuries, concurrently administering both therapies would produce additive effects.

It has been held that it is *prima facie* obvious to combine two inventions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third invention for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Moreover, with respect to the instructions that direct one how to use a kit, the US court of appeals for the Federal Circuit, *In re Ngai* 03-1524, has ruled that a kit of the prior art with a set of instructions is unpatentable (See the precedential opinion issued May 13, 2004).

Thus the invention taken as a whole is *prima facie* obvious.

Claim 8 is rejected under 35 U.S.C. 103 as being unpatentable over Baranowitz (PCT international publication WO01/08691, Reference cited in PTO-892) In view of Borgens et al. (US patent 4919140, Reference included with PTO-892) further in view of Gielen et al. (US patent 6312469, reference cited in PTO-892) Baranowitz discloses a method of regenerating tissues and organs in a mammal by causing destabilization, transdifferentiatiation, and stabilization of mammalian cells from the site of injury. (P. 5, lines 28-31, p. 8, lines 29-30) Although not mentioned specifically, the spinal cord is included within the range of organs which could be regenerated by this method. One preferred embodiment of the invention of Baranowitz includes the administration of guanosine as the agent which causes transdifferentiation. (p. 11, lines 6-7) In one embodiment, the method of Baranowitz is practiced by the administration of a treatment

capable of dedifferentiating mammalian cells, such as those described from p. 9, line 18 – p. 10, line 4 of Branaowitz, followed by the concurrent administration of guanosine (p. 11, lines 6-7) and a stabilizing agent, such as those listed on p. 11, lines 8-10. As parent claim 1 is directed to, "A method for treating a patient having a spinal cord injury, the method **comprising**: electrically stimulating the site of the spinal cord injury; and administering a purine nucleoside or analog thereof to the patient," the features of this therapeutic regimen beyond the administration of guanosine (i.e. pre-treatment of the site of injury to cause destabilization, and treatment with a stabilizing agent) are included as possible additional elements in the claimed invention. In particular, the use of trauma to destabilize the target tissue, as described on p. 10 of Baranowitz, lines 5-31, would include the surgically induced trauma involved in the implantation of an infusion pump and an oscillating field device at the site of injury, as described by instant claims 2, 3, and 8.

Although Benowitz does not explicitly specify that the endpoint of the claimed therapeutic method is one, "wherein nerve function through said injured spinal cord is at least partially restored," in the language of instant claim 1, the achievement of this therapeutic endpoint is an essential part of a successful treatment for a spinal cord injury. A therapeutic regimen which did not successfully restore nerve function through the injured spinal cord could not be said to constitute treatment of the injury. Benowitz does not teach the concurrent administration of an electrical stimulus to the site of injury, or the implantation of a device to administer guanosine to the spinal cord.

Borgens et al. discloses an oscillating field stimulation device described as, "An apparatus for stimulating nerves in the central nervous system of a mammal to regenerate within the central nervous system, comprising means for generating an oscillating electrical field with a polarity reversal period long enough to stimulate growth of cathodally facing axons of the nerves to be stimulated but less than a die back period of anodally facing axons of the nerves to be stimulated." (Claim 7) This device is intended to be used to promote the regeneration of an injured spinal cord, and falls within the limits of the terms, "electrically stimulating the site of the spinal cord injury," a device which electrically stimulates the site of the spinal cord injury," and "an oscillating field stimulation device," as they occur in the instant claims.

Gielen et al. discloses a prosthetic lamina which replaces part of the lamina bone structure. This device is, "configured for implantation adjacent to a spinal cord and an intermediate vertebral bone structure of a patient." (Claim 1) Furthermore, Gielen et al. discloses that such a prosthetic lamina may be configured with fluid channels for the delivery of a variety of medical treatments to the spinal cord. (column 6, lines 30-53)

It would have been obvious to one of ordinary skill in the art at the time of the invention to simultaneously treat a patient having suffered a spinal cord injury by administering purine nucleosides according to Baranowitz using a prosthetic drug delivery system according to Gielen et al., while also administering electrical stimulus by implanting the device of Borgens et al. into the patient.

One of ordinary skill in the art at the time of the invention would be motivated to combine the inventions in this way in order to better treat patients suffering from injury

to the spinal cord, in particular by administering a constant flow of guanosine to the site of injury while concurrently administering a second treatment to further promote regeneration. One of ordinary skill in the art would have reasonably expected that, because administration of purine nucleosides and oscillating field stimulation were both known to be useful independently for the treatment of spinal cord injuries, concurrently administering both therapies would produce additive effects. Additionally, one of ordinary skill in the art would have expected success in using the device of Gielen et al. to deliver guanosine because intrathecal drug delivery was one of the stated function of this device.

It has been held that it is *prima facie* obvious to combine two inventions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third invention for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Thus the invention taken as a whole is *prima facie* obvious.

Summary

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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